GW25-e1171

Analysis of long non-coding RNA expression patterns in cardiac fat pads of canine with atrial fibrillation

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Objectives: Long non-coding RNAs (lncRNAs) are indicated to be important orchestrators of gene regulatory networks. In this study, we aimed to characterize the lncRNA expression profiles in neural remodeling during atrial fibrillation (AF).
Methods: 6 adult beagle dogs of either sex were randomly divided into AF group (400 beats/min, right atrial pacing) and control group (without atrial pacing). After 4 weeks of tachypacing, the second-generation RNA sequencing was performed to examine the transcriptomes of lncRNAs in AF/ non-AF canine cardiac anterior right fat pads. The sequencing data were confirmed by quantitative real-time PCR (qRT-PCR). GO and KEGG pathway analyses were used to annotate the biological functions and pathways that the aberrantly expressed genes were involved in. Based on the sequence similarity, target genes of the lncRNA transcripts were predicted. Filtering pipelines were established to identify the candidate lncRNA transcripts.
Results: A sum of 61616 lncRNA transcripts was yielded by the high-throughout sequencing. Among them, 166 down-regulated and 410 up-regulated lncRNA transcripts with more than 2-fold change were identified, in which 45 transcripts were newly discovered in canine models of AF. 6 newly identified lncRNA transcripts were randomly selected and confirmed by qRT-PCR. Bioinformatic analysis showed that the aberrantly expressed genes were associated with neural growth, development, migration and neurodegenerative disorders. Additionally, based on differential expression levels, functions of the target genes, bioinformatic analysis and the tissue specific analysis, we selected two new lncRNA transcripts, TCONS_00032546 and TCONS_00026102, which might be involved in the process of neural remodeling by regulating their target genes at transcriptional level.
Conclusions: These results suggested that the dysregulated lncRNA transcripts might play a role in the initiation and development process of AF neural remodeling, which further provided potential therapeutic targets for prophylaxis and treatment of AF.

GW25-e1408

Hydrogen sulfide ameliorates High glucose-induced senescence by suppressing oxidative stress

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Objectives: In patients with diabetes, the level of hydrogen sulphide (H_2S) is remarkably decreased. And it is demonstrated that endothelial senescence is accelerated under high glucose condition. The aim of this study is to investigate the effect of exogenous H_2S on HUVEC senescence induced by high glucose.
Methods: Senescence model was established by treating HUVECs with 33 mmol/L glucose for 48 hours. Senescence was identified by β-galactosidase (SA-β gal) staining. MTT assay was used to assess cell proliferation. PAI-1, SOD1 and NF-κB p65 was analyzed by western blot. MDA level was measured using a commercial kit.
Results: High glucose induced a senescence-like phenotype in HUVECs as shown by slower proliferation, more SA-β gal positive cells and increased protein expression of PAI-1. In senescent cells, the SOD1 expression was reduced dramatically, but NF-κB p65 activity and MDA production was increased significantly. However, sodium hydrosulfide (NaHS, H_2S donor, 100 μmol/L and 200 μmol/L) was able to promote cell proliferation, decrease the number of SA-β gal positive cells and reduce PAI-1 expression. In the meantime, NaHS increased SOD1 expression, inhibited the activity of NF-κB p65 and decreased MDA production.
Conclusions: Exogenous hydrogen sulphide prevents HUVECs against high glucose-induced senescence by modulating oxidative stress and NF-κB p65 activity. Our results may indicate that hydrogen sulphide treatment would be helpful to improve endothelial function in diabetic patients. Further studies are needed to explore the value of hydrogen sulphide in clinical practice.

GW25-e2467

Expression of Neutrophil Gelatinase-associated Lipocalin in Hypotonic Contrast-induced Rat Model of Renal Injury and The Effect of N-acetylcysteine on NGAL

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Objectives: We built the rat model of contrast-induced nephropathy to observe kidney damage and the expression of neutrophil gelatinase-associated lipocalin (NGAL) in this situation. We also paid attention to the changes of NGAL level after the intervention of N-acetylcysteine (NAC), in order to know whether NGAL can be used as an index for early diagnosis of contrast-induced nephropathy (CIN), and whether NAC has renal protective effects.
Methods: Adult male SD rats of clean grade (total number 80) were randomly divided into four groups: control group (CON), contrast-induced nephropathy group (CIN), N-acetylcysteine group (NAC), and NAC plus CIN group (NAC+CIN). We collected blood samples and renal tissue of each group at the time point of 2h, 12h, 24h, 48h, and 72h after modeling (4 rats per time point of each group). Serum creatinine (Scr) values were measured by an automatic biochemical analyzer. Concentration of NGAL in serum was evaluated by Enzyme linked immunosorbent assay (ELISA) by using commercial kit. Immunohistochemistry and Western Blotting method is used to determine the expression of NGAL in renal tissue. HE-stained sections of rat kidneys were uses to assess the degree of kidney tubular injury. At the same time, renal oxidative stress was analyzed by MDA and T-SOD value.
Results: (1) Scr values: 2h, 12h and 24h after modeling, there showed no difference between the Scr values of CIN and CON group ($P>0.05$), 48h or 72h after modeling, Scr value was significantly increased in CIN group than in CON group or NAC+CIN group ($P<0.05$). There's no significantly difference between the Scr value of NAC+CIN group and CON group 48h after modeling ($P>0.05$), but difference appeared at the time point of 72h ($P<0.05$); (2) Kidney damage assessment of HE staining: 12h, 24h, 48h, 72h after modeling, different degrees of acute tubular injury occurred in CIN group, with or without epithelial cell brush border shedding, vacuolar degeneration, cell loss and regeneration, even part of tubular structural damage. At the time point of 12h, 24h, 48h or 72h, CIN group significantly showed more damage than CON group ($P<0.05$), and the damage scores of NAC+CIN group are higher than CON group too ($P<0.05$), but NAC+CIN group showed less damage than CIN group at the same time ($P<0.05$). Factorial analysis: The main effect of contrast agent was statistically significant ($F=64.128$, $P<0.01$). The interaction of contrast agents with NAC was statistically significant. (3) Serum NGAL lever: 2h, 12h, 24h, 48h or 72h after modeling, serum NGAL lever of CIN group is obviously higher than CON group ($P<0.05$), but that of NAC+CIN group is lower than CIN group ($P<0.05$). There was no difference between the serum NGAL levers of NAC+CIN group and CON group 2h after modeling ($P>0.05$). (4) Immunohistochemistry: 2h, 12h, 24h, 48h or 72h after modeling, IOD value of CIN group was significantly increased than CON group ($P<0.05$). (5) Western Blot: 2h, 12h, 24h, 48h or 72h after modeling, the NGAL level in kidney of CIN group was significantly increased than CON group ($P<0.05$). (6) Correlation analysis of tubular injury score and serum NGAL values shows that there's a positive correlation between them.
Conclusions: (1) The changes of NGAL level in both kidney and serum appears early in CIN rat model, and there's a positive correlation between tubular injury score and serum NGAL values. (2) NAC can reduce the renal tubular epithelial cell injury in CIN model, this effect may be produced through oxidative stress pathways.

GW25-e3118

Lin28a Protects Against Cardiac Ischemia/Reperfusion Injury in Diabetic Mice through the Insulin -PI3K-mTOR pathway

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Objectives: The insulin-PI3K-mTOR pathway exhibits a variety of cardiovascular activities including protection against I/R injury. Lin28a enhanced glucose uptake and insulin-sensitivity via insulin-PI3K-mTOR signaling pathway. However, the role of lin28a on experimental cardiac I/R injury in diabetic mice are not well understood. The aims of the present study were to (1) determine whether lin28a protects diabetic mice from cardiac I/R injury and (2) identify whether the underlying mechanisms of lin28a is associated with the insulin-PI3K-mTOR dependent pathway.
Methods: Diabetic mice underwent 30 minutes of ischemia followed by 3h of reperfusion. Animals were randomized to be treated with lentivirus carrying lin28a siRNA (siLin28a) or control virus (siControl), lin28a cDNA (Lin28a) or control virus (Control vector) 72h before coronary artery ligation. Myocardial infarct size, cardiac function, cardiomyocyte apoptosis and mitochondria morphology in diabetic mice who underwent cardiac I/R injury were compared between groups. The target proteins of lin28a were examined by western blot analysis.
Results: Lin28a overexpression significantly reduced myocardial infarct size, improved left ventricular ejection fraction (LVEF), decreased myocardial apoptotic index and alleviated mitochondria cristae destruction in diabetic mice underwent cardiac I/R injury. Lin28a knockdown exacerbated cardiac I/R injury as evidenced by increased infarct size, decreased LVEF, increased apoptotic index and aggravated mitochondria cristae destruction. Interestingly, pretreatment with rapamycin abolished the beneficial effects of lin28a overexpression. Lin28a overexpression increased, while Lin28a knockdown decreased the expression of IGF1R, P-Akt, P-mTOR and P-p70s6k after cardiac I/R injury in diabetic mice. Rapamycin pretreatment abolished the effects of increased P-mTOR and P-p70s6k expression exerted by lin28a overexpression.
Conclusions: This study indicates that lin28a overexpression reduces infarct size, improves cardiac function, decreases cardiomyocyte apoptosis index and alleviates cardiomyocyte mitochondria impairment after cardiac I/R injury in diabetic mice. The mechanism responsible for the effects of lin28a is associated with the insulin -PI3K-mTOR dependent pathway.

GW25-e3219

Urotensin II induces endothelial-mesenchymal transition of cardiac microvascular endothelial cells via Smad2/3 activation

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